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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/702,878	11/01/2000	Hiroshi Tamura	159-62	3533

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EXAMINER
COOK, LISA V

ART UNIT	PAPER NUMBER
1641	10

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/702,878	TAMURA ET AL.	
	Examin r	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the c ver sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *3,8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-9* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,4,5,9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I for further prosecution in Paper No. 9 filed 9/30/02 is acknowledged. Applicant traverses the Restriction Requirement because "the present invention is based on the finding that CRP binds to PC". Applicant further contends that although the methods are independent and distinct, they should be combined because of the novel CRP bound by PC link. This argument was carefully considered but not found persuasive because CRP binding to PC was previously established in the prior art. See Hokama et al.. (Journal of Reticuloendothelial Society, 1964-1973 (1973), 13(2), 111-1121 and Kishida et al. (Ensho, 1989, 9(5), 369-4290). Abstracts Only. With respect to claim 3 being a specific embodiment of a well-known sandwich method, it is noted that the utility of CRP –PC binding is not limited to the well-known sandwich method of claim 3. Therein the methods were Restricted.

2. The Restriction Requirement is still deemed proper and is therefore made **FINAL.**

3. Claims 3, 8, and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9. Currently, claims 1-2 and 4-7 are under consideration.

Priority

4. If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed copending application, specific reference to the earlier filed application (55352/1999-filed 3/3/1999 in Japan) must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph.

Drawings

5. The formal drawings submitted in this application are not objected to by the Draftsperson under 37 CFR 1.84 or 1.152.

Information Disclosure Statement

6. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 have cited the references they have not been considered.

7. The information disclosure statements filed 11/01/01 - Paper#2, filed 1/30/01 – Paper #4, filed 7/11/01 – Paper #5, and filed 9/30/02 – Paper #9 have been considered as to the merits prior to First Action.

Specification

8. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. The use of the trademarks has been noted in this application. (See for example "Xenon" page 12 line 6, "Fisher" page 17 line 13, "Triton" page 18 line 5). They should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

II. Abstract - Applicant is reminded of the proper language and format for an abstract of the disclosure. The instant Abstract uses the term "relates". "The subject invention "relates" to. Please correct.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-2 and 4-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-2 and 4-7 are vague and indefinite because it is not clear as to how the concentration of CRP will be measured if the concentrations of the starting reagents are not known. It is suggested that the method include "known" in order to obviate this rejection.

B. Claims 1-2 and 4-7 are vague and indefinite because they are drawn to a method of determining CRP concentration, but only recite the use of a labeled PC reagent. Claims 1-2 and 4-7 provides for the use of labeled PC, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

C. In claim 2 the use of the term "derived" is indefinite. As recited it is not clear if Applicant intends to mean the limitation following the term is required or is this to mean any liquid will suffice as long as it has the limitation following the term as a parent source/human being.

For example in claim 2 is the sample to be blood, plasma or serum or will the claim read on liquid compositions including the blood that has been exposed to other reagents before testing (i.e. blood placed in a lysising buffer then tested). It is suggested that the term "derived" be removed from the claims and the actual liquid embodiments be recite to obviate this rejection.

D. The term "intensity" in claim 4 is a relative term, which renders the claim indefinite. The term "intensity" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The claims are directed to concentration via intensity but do not clearly set forth how this will be done. Will comparative intensity with a control sample be conducted? If so please add to the claim.

10. Claims 1-2 and 4-7 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are explained below: The claims are drawn to an in vitro method that detects a formed complex comprising an analyte (CRP) and a specific binding partner (labeled PC) in a liquid medium. Merely reciting an in vitro method (claim 1) is not considered a proper method. The claims require at least the contact are reagents to form a binding complex of interest, the separation of bound from unbound materials, detection of the labeled complex, and a correlation of the measured complex to the analyte of interest. As recited the claims do not include a contact step, binding step, detection or correlation. Please include the appropriate assay steps.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-2 and 4-7 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure, which is not enabling. The methods of claims 1-2 and 4-7 have insufficient steps. The process is deemed critical or essential to the practice of the assay method in the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). There are no claimed steps reciting the washing/removal of unbound or bound material. For example, in claim 1, the mere use of a labeled PC will always result in a positive measurement. A separation step that removes unbound/bound solution from the analyte/sbp – CRP/Labeled PC complex formed is missing. If you do not have a separation step after complex formation, the mixing of the analyte with the spb will not in it self measures the degree of association. A labeled spb will always provide a positive result regardless of the analyte/sbp complex and thus could not be utilized to detect an analyte. The presence of the unbound mixture is also a serious problem in view of the quantification of the analyte present in a sample. The presence of the unbound label will generate a greater detection signal as for the analyte measurement, than is actually present. Please add the removal of unbound label or bound material for further analysis to the claims or clearly indicate the specific method of detection that does not employ the removal of unbound/bound material.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1, 2 and 4 are rejected under 35 U.S.C. 102(a) as being anticipated by Liberda et al. (Chimia, 53, 1999, 528-532).

Liberda et al. disclose biotinlylated and FITC labeled phosphorylcholine (PC). CRP is taught as the most studied phosphorycholine-binding protein. See abstract and Introduction. Tests were conducted on seminal plasma of different species. See page 529, 1st column, 1st paragraph.

II. Claims 1, 2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Heggli (GB 2 217 335 A).

Heggi disclose a method of measuring CRP (c reactive protein) via binding to phaophoryl choline (PC) residues and/or aminoethyl dihydrogen phosphate (AEDP). See abstract and claims. Enzymes labeled with PC or AEDP are employed to generate a detectable measurement indicative of the bound CRP. See page 6. The method was tested on serum and plasma samples. Page 3.

III. Claims 1, 2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Hokama et al. (Journal of Reticuloendothelial Society, 1964-1973), 1973, 13(2), 111-121). Abstract Only.

Hokama disclose a method of phosphorylcholine thymidine leukocyte via C-reactive protein binding. See abstract.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liberda et al. (Chimia, 53, 1999, 528-532), Heggli (GB 2 217 335 A), or Hokama et al. (Journal of Reticuloendothelial Society, 1964-1973), 1973, 13(2), 111-121) Abstract Only in view of Hemmila et al. (Analytical Biochemistry, 137, 335-343, 1984).

Please see Liberda et al., Heggli, or Hokama et al. as set forth above.

Liberda et al., Heggli, or Hokama et al. differ from the instant invention in failing to teach Eu as the label to PC.

However, Hemmila et al. teach europium as a label in time-resolved immunofluormetric assays/method. See abstract. The lanthanide, europium(III) is taught to form highly fluorescent chelates with many different organic ligands. The lanthanide has been used a fluorescent probes in the study of Ca-binding sites enzymes, proteins, and in the measuring of nucleic acid conformation. See pages 335, 1st column. In this study europium was detected and quantified after an immunoreaction. Page 336, 1st paragraph. Europium could be utilized as the labels with an antibody, antigen, or hapten. See page 342, 1st column 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a europium compound as taught by Hemmila et al. to label PC in the CRP-PC binding assay/methods of Liberda et al., Heggli, or Hokama et al. because Hemmila et al taught that the long fluorescent decay time of the label (europium) makes it suitable as a label in the measurement of biospecific affinity reactions. Further the use of europium as a label in time-resolved fluoroimmunoassays makes it possible to achieve highly sensitive measurements, which incorporate the positive features of FIA but avoid the drawbacks of RIA. Page 335 2nd column. Further the europium label is stable, involves no radioactivity, and requires a counting time of only 1 second. See page 342, last paragraph.

14. For reasons aforementioned, no claims are allowed.

Remarks

15. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Kishida et al. (Ensho, 1989, ((5), 369-74 Abstract Only) teach a method of evaluating the binding specificity of Human C-reactive protein and phosphorycholine with affinity chromatography.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
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4/6/03

LONG V. LE
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04/07/03